



US007253177B2

(12) **United States Patent**
Lin et al.

(10) **Patent No.:** **US 7,253,177 B2**
(45) **Date of Patent:** **Aug. 7, 2007**

(54) **SYNTHESIS AND ANTIMALARIAL
ACTIVITY OF
PYRROLO[3,2-F]QUINAZOLINE-1,3-DIAMINE
DERIVATIVES**

(75) Inventors: **Ai J. Lin**, Potomac, MD (US); **Jian
Guan**, Olney, MD (US); **Quan Zhang**,
Rockville, MD (US); **Donald R.
Skillman**, Silver Spring, MD (US)

(73) Assignee: **United States of America as
Represented by the Secretary of the
Army**, Washington, DC (US)

(*) Notice: Subject to any disclaimer, the term of this
patent is extended or adjusted under 35
U.S.C. 154(b) by 272 days.

(21) Appl. No.: **10/971,846**

(22) Filed: **Oct. 22, 2004**

(65) **Prior Publication Data**

US 2006/0094736 A1 May 4, 2006

(51) **Int. Cl.**

A01N 43/54 (2006.01)

A61K 31/505 (2006.01)

C07D 239/00 (2006.01)

C07D 471/00 (2006.01)

C07D 487/00 (2006.01)

C07D 491/00 (2006.01)

(52) **U.S. Cl.** **514/267**; 544/247

(58) **Field of Classification Search** 544/247;
514/267

See application file for complete search history.

(56) **References Cited**

U.S. PATENT DOCUMENTS

4,118,561 A * 10/1978 Ledig 544/250
4,208,520 A 6/1980 Ledig et al.

FOREIGN PATENT DOCUMENTS

WO WO/02/068425 A 9/2002

OTHER PUBLICATIONS

Ho-Sam Ahn, et al., Structure-Activity Relationships of Pyr-
roloquinazolines as Thrombin Receptor Antagonists, Bioorganic &
Medicinal Chemistry Letters 9 (1999) 2073-2078.*

* cited by examiner

Primary Examiner—Zachary C. Tucker

Assistant Examiner—Erich A. Leeser

(74) *Attorney, Agent, or Firm*—Elizabeth Arwine

(57) **ABSTRACT**

The invention relates to derivatives of pyrroloquinazolinedi-
amine, more specifically derivatives of 7-(substituted)-7H-
pyrrolo[3,2-F] quinazoline-1,3-diamines that are non-toxic
and are also effective in the treatment of malaria, including
P. falciparum and *P. vivax* strains. The derivatives are certain
carbamate derivatives, succinimide derivatives, alkylcar-
boxamides derivatives and acetamide derivative, phthalim-
ides, alkylamines and all other amide and imide derivatives
and their 1-hydroxy analogs. The derivatives of the present
invention are also soluble in common organic solvents to
facilitate the purification in a large scale synthesis of the
composition.

66 Claims, 2 Drawing Sheets